CHEMISTRY LETTERS, pp. 1069-1072, 1983. © The Chemical Society of Japan 1983

STRUCTURES OF SESTERTERPENOIDS FROM THE SCALE INSECT CEROPLASTES CERIFERUS. REVISION OF THE 14-MEMBERED CERIFERENE SKELETON FROM 2-t/6-c/10-t TO 2-c/6-t/10-t

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The structures of two new macrocyclic sesterterpenoids ceriferol-I **1** and ceriferic acid-I **2** isolated from the secretion of the scale insect Ceroplastes ceriferus were determined. The results led to the revision of the arrangement of annular double bonds in the carbon skeleton (from **1a** to **1**) of all compounds correlated in the previous reports.

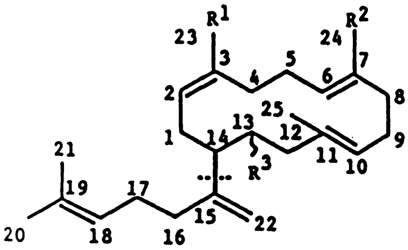
During our investigation of the sesterterpenoids produced by the scale insect Ceroplastes ceriferus Anderson (Coccidae), collected in Osaka Prefecture, Japan, in March 1982, two new sesterterpenoids were isolated by a previously described procedure:[1] Ceriferol-I **1**, colorless oil, $C_{25}H_{40}O$ (M^+ 356.308), $[\alpha]_D^{24}$ - 83° (c, 1.8, $CHCl_3$); ceriferic acid -I, colorless oil as methyl ester **2**, $C_{26}H_{40}O_2$ (M^+ 384.303), $[\alpha]_D^{24}$ - 93.5° (c, 2.0, $CHCl_3$). The two other minor constituents were identical with ceriferol **3**[3,4] and ceriferic acid **4** (Fig. 1).[3,4]

It was apparent from comparison of ^{13}C NMR chemical shifts that ceriferol-I **1** and methyl ceriferate **2** were closely related to the previously reported ceriferol **3** and ceriferic acid methyl ester **4**, respectively.[3,4] Cericerene **5** obtained from ceriferol-I **1** in the present study was identical in all respects with that obtained from cericerol-I **6**,[1] confirming that the geometry of the double bonds and their arrangement as well as their absolute configuration at C-14 (R) are the same in the two series of compounds. The steric effect on ^{13}C NMR chemical shifts in the geometry of double bonds is well established;[1] comparisons of methyl chemical shifts of various compounds (Table 1) with those in cericerene **5** (C-20 δ 25.7, C-21 δ 17.8, C-23 δ 22.5, C-24 δ 15.6, C-25 δ 15.5 ppm) indicate the presence of one cis and two trans double bonds within the macrocyclic ring. Since the 22.5 ppm signal in cericerene **5** (due to methyl on cis double bond) is replaced by hydroxymethyl signals (at 66.6 ppm) in ceriferol-I **1** and ceriferol **3**, the $-CH_2OH$ group is on the cis double bond in these two.

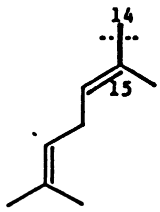
In order to establish the arrangement of double bonds within 14-membered ring, ^1H NMR's (360 MHz) with sequential lanthanide shift reagent [$Eu(fod)_3$] additions were used on **1** and **3**. Subsequent application of homonuclear difference decoupling to the protons thus separated gave rise to the partial structures **1** and **3** shown in Fig. 3. Ceriferol **3** was heteronuclearly decoupled at 14-H (2.82 ppm, after addition of shift reagent), upon which C-14 (47.0 ppm) in the ^{13}C NMR off-resonance spectrum collapsed from a doublet to a singlet insread of a triplet to a doublet which would have occurred in the case of the structure **3a** (Fig. 3). Although the presence of a long-range coupling[4] between 2-H (7.75 ppm) and C-14 was not observed in this case, the above evidence confirms the partial structures **1** and **3** (Fig. 2).

† Visiting Scientists in 1982.

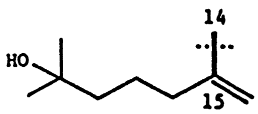
Thus, the current studies lead to the conclusion that the skeletal structure of all sesterterpenoids isolated from *C. ceriferus* and correlated directly or indirectly with cericerene 5 ("cericerenes") should be changed from 2-*t*/6-*c*/10-*t*[1-3] to 2-*c*/6-*t*/10-*t* (Ia → I); this arrangement is the same as that of the structure proposed for albocerol,[5] the absolute configuration of which remained to be elucidated. Cericerene with the wrong 2-*t*/6-*c*/10-*t* geometry 5a has been synthesized by Kato and co-workers.[6] The synthetic specimen is not identical with cericerene 5.



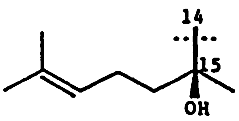
* 1 ceriferol-I (R^1 = CH_2OH, R^2 = Me, R^3 = H)
* 2 ceriferic acid -I (Me) (R^1 = COOMe, R^2 = Me, R^3 = H)
5 cericerene (R^1 = R^2 = Me, R^3 = H)
6 cericerol-I (R^1 = Me, R^2 = CH_2OH, R^3 = H)
8 cericeroic acid (Me) (R^1 = Me, R^2 = COOMe, R^3 = H)
9 13-methoxy cericerene (R^1 = R^2 = Me, R^3 = OMe)
10 13-ethoxy cericerene (R^1 = R^2 = Me, R^3 = OEt)



3 ceriferol (R^1 = CH_2OH, R^2 = Me, R^3 = H)
4 ceriferic acid (Me) (R^1 = COOMe, R^2 = Me, R^3 = H)
11 α-cericerene (R^1 = R^2 = Me, R^3 = H)
12 α-cericerol-I (R^1 = Me, R^2 = CH_2OH, R^3 = H)



13 18-dihydro-19-hydroxycericeroic acid (R^1 = Me, R^2 = COOMe, R^3 = H)



7 cericerol-II (R^1 = Me, R^2 = CH_2OH, R^3 = H)
14 15,23-dihydroxy cericerene (R^1 = CH_2OH, R^2 = Me, R^3 = H)

Fig. 1. "Cericerenes" from *C. ceriferus* (* indicate newly isolated compounds)

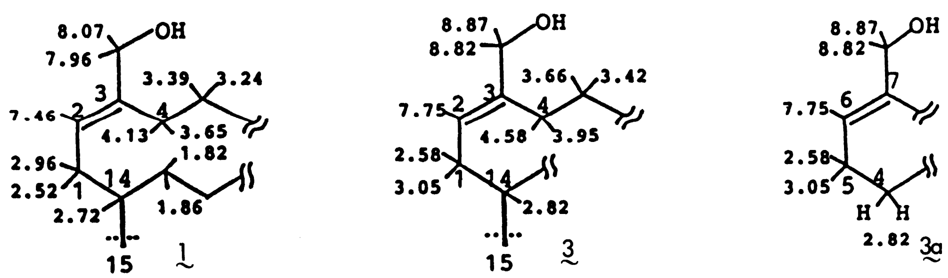
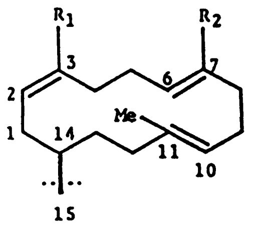


Fig. 2. Partial structures of compounds 1 and 3 (^1H NMR, 360 MHz in $CDCl_3$) after 48% and 30% Meq. $Eu(fod)_3$-d_{27} addition, respectively. Partial structure 3a is based on skeleton Ia.

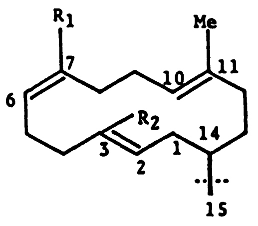
Table 1. ^{13}C NMR chemical shifts (δ) of compounds 1, 2, 3, 4, 14, 5, 11, 9, 10, 6, 12, 7, 8, 13, 6-acetate, 12-acetate, and 7-acetate in $CDCl_3$. Assignment based on lanthanide shift study on 3, and by correlation with similar compounds. a - f assignments may be reversed within each column.

C-No.	1	2	3	4	14	5	11	9	10	6	12	7	8	13	6-acetate	12-acetate	7-acetate
1	30.6[a]	30.7	29.6	29.8[a]	28.4[a]	30.5[a]	30.4	30.8[a]	30.8[a]	30.7[a]	30.0[a]	29.1[a]	30.7[a]	30.4[a]	30.7[a]	30.3[a]	29.2[a]
2	127.4	141.9	127.6	142.4	127.5	125.1[b]	125.2[a]	129.3	128.5	125.3[b]	125.9	126.4[b]	125.7	125.4	125.5[b]	125.8	126.4[b]
3	137.8	131.3[a]	137.6	131.3[b]	137.8	134.1[c]	133.8[b]	132.7[b]	133.3[b]	133.3[c]	133.4[b]	134.2[c]	133.9[b]	133.6[b]	133.4[c]	133.2[b]	134.4[c]
4	27.3	26.8	27.2	26.9[c]	26.6	31.1[a]	29.4	31.0[a]	30.9[a]	30.3[a]	29.5[a]	28.3[a]	30.4[a]	30.1[a]	30.3[a]	29.4[a]	28.4[a]
5	24.5[b]	26.4	24.6[a]	26.0	24.8[b]	24.6[d]	24.5[c]	24.0	23.9	24.1[d]	24.3[c]	24.4[d]	25.6[c]	25.3[c]	24.4[d]	24.4[c]	24.4[d]
6	125.2[c]	125.3[b]	124.7	125.3[d]	125.6[c]	125.1[b]	124.9[a]	125.3	125.4	128.6	129.1	129.2	141.6	141.4	131.5	131.7	132.0
7	133.3[d]	133.6	133.3[b]	133.7[e]	133.7[d]	133.0[c]	133.1[b]	134.9[b]	134.7[b]	136.5	136.9	136.5	130.2	129.9	131.5[e]	131.7[d]	131.4[e]
8	36.1	36.2	35.8	36.0	39.0[e]	36.2	35.8	36.3	36.3	35.6[e]	35.9[d]	35.1	35.5	35.2[d]	36.1	35.9	35.4
9	30.7[a]	31.8	29.9	31.2[a]	28.9[a]	31.4[a]	31.0	31.4[a]	31.3[a]	31.0[a]	31.1[a]	30.3[a]	30.8[a]	30.6[a]	31.0[a]	30.9[a]	29.9[a]
10	124.8[c]	124.3[b]	125.0[c]	125.4[d]	125.6[c]	125.0[b]	124.9[a]	121.4	121.5	124.8[b]	124.9[e]	126.0[b]	124.4[d]	124:2	124.4[b]	124.6[e]	125.4[b]
11	132.9[d]	132.6	133.1[b]	132.9[e]	132.7[d]	132.9[c]	132.9[b]	133.3[b]	133.3[b]	133.1[c]	133.6[b]	134.2[c]	133.2[b]	132.9[b]	133.4[c]	133.7[b]	133.9[c]
12	40.2	40.1	40.2	40.3	39.8[e]	40.3	40.2	31.4[a]	31.6[a]	36.0[e]	35.7[d]	39.0	36.2	35.9[d]	36.1	36.1	39.1
13	24.6[b]	24.3[c]	24.5[a]	24.5	24.0[b]	24.6[d]	24.5[c]	88.3	86.4	24.6[d]	24.6[c]	24.7[d]	26.0[c]	25.7[c]	24.7[d]	24.8[c]	24.8[d]
14	44.3	43.4	46.4	49.9	46.8	44.6	46.6	44.1	44.1	44.5	46.9	47.2	44.7	44.2	44.7	46.9	47.2
15	152.5	151.9	136.8	136.4	75.3	153.0	137.1	153.2	153.2	152.4	137.1	75.7	152.5	152.2	152.6	137.1	75.4
16	33.5	33.8	123.5	123.4	39.9[d]	33.7	123.7	34.1	34.1	33.4	123.6	39.9	33.5	33.8	33.5	123.6	39.7
17	26.4	25.8[c]	26.9	26.9[c]	22.0	26.6	26.8	26.7	26.7	26.4	26.8	22.2	26.5	22.3	26.5	26.9	22.1
18	124.7[c]	124.2[b]	124.8[c]	124.6	124.6	124.6	124.5	124.6	124.5	124.2	124.7[e]	124.7	124.4[d]	43.6	124.7[b]	124.6[e]	124.6
19	131.5	131.1[a]	131.2	131.1[b]	131.2	131.3	131.0	131.4	131.5	131.1	131.2	131.5	131.2	70.3	131.2[e]	131.7[d]	131.4[e]
20	25.7	25.5[c]	25.6	25.7	25.5	25.7	25.6	25.7	25.6	25.6	25.6	25.7	25.6	28.9[e]	25.6	25.7	25.6
21	17.7	17.6	17.7	17.7	17.5	17.8	17.7	17.8	17.7	17.7	17.8	17.7	17.6	28.9[e]	17.6	17.8	17.6
22	109.2	109.5	12.1	12.3	23.7	108.9	12.0	108.9	108.8	108.7	12.1	23.6	109.0	108.7	109.0	10.9	24.0
23	66.6	168.2	66.6	168.4	65.9	22.5	22.4	22.5	22.5	22.4	22.4	22.2	22.4	22.1	22.3	22.4	22.1
24	15.5[e]	15.3[d]	15.4[d]	15.6[f]	15.3[f]	15.6[e]	15.6[d]	15.4	15.4[c]	59.7	60.0	59.8	168.5	168.3	61.5	61.7	61.7
25	15.5[e]	15.1[d]	15.6[d]	15.3[f]	15.2[f]	15.5[e]	15.4[d]	9.8	10.0	15.3	15.6	15.5	15.3	15.1	15.3	15.7	15.4
		51.5		51.3				55.4	62.7				51.0	50.8	170.9	170.9	170.9
									15.4[c]						20.9	21.0	20.9

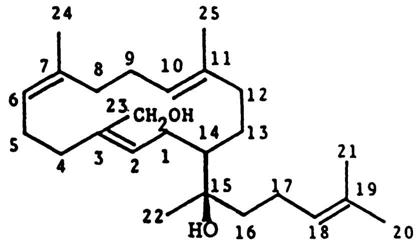
The erroneous earlier conclusion[1-3] that cericerol-II[1] should be represented by structure **7a** was deduced from the following observations: cericerol-II **7** (**7a**), which was converted to cericerol-I **6** (**6a**), exhibited signals due to hydroxymethyl protons at 3.80 and 4.25 ppm (each 1H, d, J = 12 Hz) with large differences in chemical shifts at 3.89 and 4.12 ppm in **6** (**6a**) which was interpreted to suggest a location close to the additional 15-hydroxyl group of **7a**. Secondly, the observation that ceriferic acid **4a** and the tosylate of ceriferol **3a** both showed no CD Cotton effect was interpreted to indicate[3] that the chromophores were remote from the C-14 chiral center. This lack of Cotton effect in acid **4** is probably due to the fact that the -COOH group is fortuitously in a symmetric environment;[7] the tosylate of **3** is presumably not influenced by C-14 or the chiral ring environment because of the intervening CH_2 group. In the present study, ceriferic acid benzylamide, in fact, proved to show a Cotton effect at 213 nm (hexane) $\Delta\epsilon$ - 1.4. The skeleton forwarded by Kusumi, et al.[4] for ceriferic acid **4** has thus turned out to be correct.



1 2-c/6-t/10-t



1a 2-t/6-c/10-t



6a (15,22-anhydro)
7a

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4) T. Kusumi, T. Kinoshita, K. Fujita, and H. Kakisawa, Chem. Lett., 1979, 1129.
5) R. Veloz, L. Quijano, J.S. Calderon, and T. Rios, J. Chem. Soc., Chem. Commun., 1975, 191.
6) See the following communication, we are grateful to Dr. Kato for this information.
7) The 14-membered ring must adopt an asymmetric conformation because of the chiral center C-14. However, the spatial arrangement of double bonds at C-6, C-10, and other groups may be such that their chiral influence on the chromophore accidentally cancels out.

(Received May 4, 1983)